

50X1-HUM

**Page Denied**

Next 2 Page(s) In Document Denied

Summary from the report of the Psychiatric Department of the University of J.E.Purkyně, Brno. Director: prof.MUDr.J.Hádlík

Therapeutic trials of the new czechoslovak preparation Phenoharmane

K. Náhunek, A.Rodová, J.Bojanovský

Phenoharmane was administered at the psychiatric department in Brno to a total number of 35 psychotic subjects /28 women, 7 men/. The age of the patients varied from 15 to 68 years. In spite of the diagnostic inhomogeneity of the treated group there was a uniform trend in all cases with minor exceptions only. They all represented an acute course of the first attack of the illness or an exacerbation of the periodically recurring psychosis with a prevalently good prognosis.

Phenoharmane was administered at daily doses of 250-1500 mg orally, in cases of manic syndromes intramuscular injections at maximum doses of 150 mg were used at the same time. In manic syndromes daily doses of the drug fluctuated about 1 gr daily, often they were even higher. In one case of schizophrenia the treatment was combined with pentazol convulsions. The duration of the treatment was 6-33 days. Before and during the treatment the GOT, GPT and alkaline phosphatase in serum were controlled together with the leukogram, routine urine investigation, sedimentation rate etc. at regular intervals. Therapeutic results are summarized in table No. 1.

Tab.No 1.

Diagnosis	therapeutic results classified according to the Serejsky method					total
	A-B	C	D,	O	-	
Schizophrenia	4	3	1	7	1	16
Paraphrenia	1	-	2	1	-	14
Manic syndromes	1	1	-	4	5	11
✓ Deranged behaviour	2	1	-	-	-	3
Huntington's chorea	-	1	-	-	-	1
Total	8	6	3	12	6	35
%	22,8	17,1	8,7	34,3	17,1	

At the first glance the table shows the relatively low therapeutic value of the drug. The transient dysphorizing effect of the drug was observed in 3 from 11 subjects. Very interesting was the favourable effect in some derangements of behaviour in adolescent subjects which was nevertheless in one case controlled also by placebo. All three cases showed dissociability effects as mendacity, loss of discipline, angry and refractory reactions, representing always educational problems. The number of such cases is however too small to allow definite conclusions. A double blind test is needed to meet the problem of the effectiveness of the drug in similar cases. In one case of Huntington's chorea Phenoharmane caused a reduction of hyperkinesia and tremor to approximately the same degree as successive administration of reserpine. More trials in some other hyperkinesias as in chorea minor are suggested.

Side-effects observed during the treatment with Phenoharmane were toxic morbilliform eruptions in one case, uncharacteristical headaches in two cases. The extrapyramidal symptomatology known to occur during the treatment with reserpine was not observed. Values of GOT, GPT, alkaline phosphatase, Takata turbidity reaction, and leukogram were essentially normal. In one case of schizophrenic women in which the treatment with Phenoharmane was combined with convulsions a prolonged apnoic pause with a collapse of short duration was provoked by the pentazol convulsion. The patient recovered spontaneously. This case recalled of the previously described complications of the combined reserpine and electroshock therapy. It is therefore recommendable to bear in mind this danger and not to combine Phenoharmane with the convulsion therapy.

All subjects which showed an insufficient effect after the Phenoharmane administration were treated with other drugs as chlorpromazine, reserpine or in several cases with thioridazine and perphenazine. From 24 subjects this therapy caused full recovery in 18 /type of remission A-B/, partially recovered 4 /type C/ and unchanged remained 2.

If the experiments with the immediate results of the Phenoharmane treatment are summarized in an intraindividual comparison with currently used neuroleptics, so Phenoharmane presents itself as a relatively less effective and less suitable drug for the monotherapy of psychotic cases. The dysphorizing effect of the drug could be with difficulties only employed in the the-

rapy of manic syndromes owing to its insufficient influence on the psychomotor component which makes a more effective therapy necessary in a short time. Further therapeutic trials are suggested in the above mentioned cases of deranged behaviour in adolescents and in some extrapyramidal hyperkinesias, e.g. chorea minor. Some consideration deserves also the previously demonstrated interference of Phenoharmine with the metabolism of serotonin which could possibly be employed in some combined treatments with monoamine oxidase inhibitors, such trials being now in progress at this clinic.

### References to Phenoharmane

- 1/ Protiva M. et al., Synthetic models of hypotensive alkaloids. 1.1-aralkyl-1,2,3-tetrahydronorharmane group. Chem. Listy 51, 1915, 1957 /in czech/.
- 2/ Trčka V., Vaněček M., Hypotensive effects of 1-substituted 1,2,3,4-tetrahydronorharmanes. Chemotherapeutics and their evaluation. Summaries of papers read at the Pharmaceutical Symposium, Praha 3-7.9.1956. Edited by the Pharmaceutical Section of the Cz. Med. Soc. of J.E. Purkyně, p. 72 /in czech/.
- 3/ Vinař O., New trends in the psychiatric pharmacotherapy. Read at the Regional Psychiatric Seminar in Brno, 24.5.1958. Farmakoterapeutické zprávy OIS, 4, 171, 1958 /in czech/.
- 4/ Vinař O., New psychotropic drugs. Read at the Psychiatric Seminar in Lázně Jeseník, 9.1.1959. /in czech/.
- 5/ Dlabač A., Macek K., Vaněček M., Trčka V., Reserpine-like effect of Phenoharmane. Čs. Fysiol., 8, 177, 1959 /in czech/.
- 6/ Horácková E., Vojtěchovský M., Experiences with the Clyde's method designed to reflect the changes of emotionality under the influence of tranquillizers and psychostimulants. Read at the Psychiatric Seminar in Lázně Jeseník, 7.1.1960 /in czech/.
- 7/ Dlabač A., The effect of Phenoharmane and cyanacethydrazide from the standpoint of 5-hydroxytryptamine and inhibition of aminooxylase. Dissertation 1960, VUFB /in czech/.
- ✓ 8/ Vinař O., Phenoharmane in psychiatry. Preliminary report. Discussion at the Internat. Congr. of Psychiatry in Basel, 10.7.1960. STAT
- 9/ Vinař O., The use of a new Czech preparation Phenoharmane in psychiatry. Čas. Lék. Čes., 99, 1422, 1960 /in czech/.
- 10/ Vítek V., Vojtěchovský M., Ryšánek K., Kuhn E., Comparison of the effects of Phenoharmane and reserpine on the metabolism of serotonin, tryptamine, energy metabolism and central nervous activity. Aktiv. Nerv. Sup., 2, 360, 1960 /in czech/.
- 11/ Náhunek K., Rodová A., Hojanovský J., Therapeutic trials with a new Czech preparation Phenoharmane. Čsl. psychiatrie, 1961 - in print /in czech/.

211-59

Phenoharmene, a new dysphoria producing drug

Oldřich V i n a ř

/Institute for Postgraduate medical Education, Prague./

Phenoharmene is a brand of benzyltetrahydronorharmene, representing a simplified model of reserpine. It was synthesised by Protiya and its pharmacological properties were investigated by Trčka and coll. The compound possesses in lower doses some effects of reserpine character /enhances excretion of 5-HIAA and potentiates Thiopentale anaesthesia in mice, causes a ptosis, fall of temperature etc./, in higher doses shows convulsive effects.

Clinical trials were made on 32 subjects, including 19 manic-depressives psychoses in the manic phase, 1 manic syndrome in progressive paralysis, 10 schizophrenics and 2 psychomotor excitations in psychogenic psychoses. Control studies with placebo designed as double blind test were not undertaken. 5 subjects were their own control, when relapse followed the interruption of the treatment. The doses of 200 - 900 mg were administered *per os* daily for a period from 10 days to 2 months. Phenoharmene is practically a nontoxic drug, and no particular side effects were observed during its administration.

Best results were found in manic conditions. From 19 treated subjects a complete cure was attained in 12. In 8 of these subjects the cure is especially quick, being effected in a period of 10 days. In other 2 subjects favourable influence was also observed, especially in the emotional component of the disease: the elation disappeared, nevertheless the psychomotor excitation was only insignificantly influenced. Instead of the euphoria a morosity and reasoning was observed. One case of manic syndrome in progressive paralysis /general paralysis/ showed disappearance of euphoric states, whereas the hyperactivity was inhibited only partially. In 5 cases of 10 schizophrenics Phenoharmene was completely without effect and in another 5 cases the effect was not very pronounced, causing only some shift

in the symtomatology in the direction of the depression.

As primary indication of Phenoharmame figures the manio syndrome, which dissociates under its influence in its enhanced psychomotor activity and the proper affective componente. Phencharmane affects selectively the mood, whereas the psychomotor component is only insignificantly influenced. It is observed especially after the i.v. administration, when a glad and happy person changes during the injection in a very unhappy, depressed and anxious one, beginning even to weep. This state is in contrast with the preserved excited mimics and behaviour.

Inasmuch as Imipramine is called a thymoleptic drug, then Phenoharmame could be designed as a dysphoric drug. Both drugs are selectively affecting the emotions and act as mutual antagonists. Even if in the future the Phenoharmame will not appear clinically usefull, neverthelless its effects are interesting enough from the standpoint of theorectical investigation.

---

x/

Research Institute for Pharmacy and Biochemistry, Prague